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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/550,381	09/21/2005	David Aitken	PN/4-33001A	3366

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NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
ZAREK, PAUL E	

ART UNIT	PAPER NUMBER
4161	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/550,381	AITKEN ET AL.	
	Examiner	Art Unit	
	PAUL ZAREK	4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,9,10 and 13* is/are pending in the application.

4a) Of the above claim(s) 9 is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,10 and 13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *09/21/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 8, 11, and 12 have been canceled by the Applicant. Claims 1-7, 9, 10, and 13 are currently pending. This is the first Office Action on the merits of the claim(s).

Election/Restrictions

2. Applicant's election of Group I in the reply filed on 07/07/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

4. Applicant's election of two anti-epileptic drugs, carbamazepine and a derivative of formula I, wherein R_1 is hydroxy, R_2 is hydrogen, R_3 is nitro and X is methylene (disclosed as compound 1 on page 12 of the specification) in the reply filed on 07/07/2008 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 1-7, 10, and 13 read on the elected species.

Priority

5. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. The effective filing date of the instant application is 04/02/2004.

6. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. The date of foreign priority of the instant application is 04/04/2003.

Information Disclosure Statement

7. The information disclosure statement filed 09/21/2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 112 (2nd paragraph)

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-7, 10, and 13 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential structural cooperative relationships of elements, such omission amounting to a gap between the necessary structural connections. See MPEP § 2172.01. The

omitted structural cooperative relationships are: how a combination comprising two anti-epileptic drugs can be administered in a fashion other than simultaneously. A combination of drugs necessarily indicates that the drugs will be administered at the same time. Separate and sequential administration necessarily indicates that the drugs will be administered at different times and are thus not a combination. Therefore, Claims 1-7, 10, and 13 are lacking essential structural elements rendering the claimed invention indefinite.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Czuczwar, et al. (European Journal of Pharmacology, 1998), in view of Deckers (CNS Drugs, 2002), and Suter, et al. (Mutation Research, 2002).

13. Claims 1-7 of the instant application are drawn to a combination comprising two anti-epileptic drugs for simultaneous, separate or sequential use. Claim 2 limits the combination to a combined preparation. Claims 3-7 limit the carboxamide (Claim 3) to carbamazepine (Claim 6), and the AMPA antagonist (Claim 4) to a derivative of formula I (Claims 5 and 7). Claim 13 is drawn to a kit comprising a combination of two anti-epileptics in a unit dosage form for simultaneous, separate or sequential administration.

Czuczwar, et al., teach a combination of carbamazepine and LY300164, a dual AMPA/kainate receptor antagonist, in pharmaceutical compositions administered sequentially to mice in a murine model of epilepsy (Table 1). Czuczwar, et al., does not teach the combination of carbamazepine and the elected AMPA receptor antagonist, which is known in the art as AMP397.

Suter, et al., teach that AMPA receptors are involved in the initiation and propagation of seizures (pg 181, col 2) and that AMP397 is a selective AMPA receptor antagonist and a potent anticonvulsant (pg 182, col 1, sentence 1). Carbamazepine slows the rate of recovery of voltage activated Na^+ channels from inactivation. Deckers teaches that both sequential monotherapy and polytherapy are good options for the treatment of epilepsy (pg 162, section 5 "Conclusions"), indicating that anti-epileptic drug combinations (simultaneous, sequential or separate) are well known in the art. Deckers also teaches that when adding a second anti-epileptic to a treatment regimen, it is advantageous to choose a drug with a different mechanism of action than the first (pg 162, section 4.3). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Czuczwar, et al., and

Deckers and Suter, et al., to create an anti-epileptic drug combination comprising carbamazepine and AMP397.

14. Claims 1-7, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Levy, et al. (US Patent No. 5,095,033, 1992) in view of Deckers and Suter, et al.

Claim 1 of the instant application are drawn to a combination comprising two anti-epileptic drugs for simultaneous, separate or sequential use. Claim 2 limits the combination to a combined preparation. Claims 3-7 limit the carboxamide (Claim 3) to carbamazepine (Claim 6), and the AMPA antagonist (Claim 4) to a derivative of formula I (Claims 5 and 7). Claim 10 of the instant application is drawn to a pharmaceutical composition comprising two anti-epileptic drugs.

Levy, et al., teach a preferred embodiment of a pharmaceutical composition comprising stiripentol and carbamazepine for the treatment of epilepsy. Stiripentol is an anti-epileptic drug that increases GABAergic transmission. Levy, et al., do not teach the combination of the elected species (carbamazepine and AMP397). Deckers teaches that when adding a second anti-epileptic to a treatment regimen, it is advantageous to choose a drug with a different mechanism of action than the first (pg 162, section 4.3). Suter, et al., teach that AMPA receptors are involved in the initiation and propagation of seizures (pg 181, col 2) and that AMP397 is a selective AMPA receptor antagonist and a potent anticonvulsant (pg 182, col 1, sentence 1). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the teachings of Levy, et al., to incorporate the teachings of Deckers and Suter, et al., to formulate an anti-epileptic pharmaceutical composition comprising carbamazepine and AMP397. Therefore, it would have been *prima facie* obvious to one of

ordinary skill in the art at the time the invention was made to take the combination medication of carbamazepine and stiripentol) and substitute another known anticonvulsant, the instant species AMP397, for stiripentol.

15. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Czuczwar, et al., and Deckers and Suter, et al., as applied to claims 1-7 above, and further in view of Weaver, et al. (US Patent No. 6,306,909, 2001).

16. Claim 13 is drawn to a kit. Applicant defines "kit" as comprising "the first and second active ingredient . . . [that] can be dosed independently or by use of different fixed combinations with distinguished amounts of the ingredients, i.e., simultaneously or at different time points." (pg 4, paragraph 3, lines 1-4). Applicant, therefore, has defined a "kit" to comprise two anti-epileptic drugs to be administered either in a polytherapy fashion (simultaneous delivery) or sequential monotherapy manner (different time points). Czuczwar, et al., Deckers, and Suter, et al. teach a combination of carbamazepine and AMP397, but do not disclose the combination of the two anti-epileptic drugs as part of a kit.

17. Weaver, et al. teach that kits comprising an anti-epileptic drug to provide a convenient means of administering the drug. (col 9, lines Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Czuczwar, et al., and Deckers and Suter, et al., to create a kit comprising an anti-epileptic drug combination comprising carbamazepine and AMP397.

Conclusion

18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to PAUL ZAREK whose telephone number is (571) 270-5754. The examiner can normally be reached on Monday-Thursday, 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, PATRICK NOLAN can be reached on (571) 272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

PEZ

/Patrick J. Nolan/
Supervisory Patent Examiner, Art Unit 4161